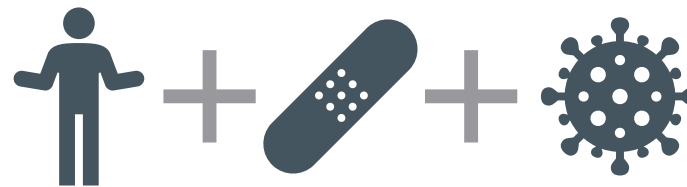




PrEP science update: “**Latest evidence and innovations**”



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What is PrEP?

Pre-exposure prophylaxis (PrEP) is the use of antiretroviral medications by people without HIV before potential HIV exposure to prevent acquisition.

- Key principle: PrEP is highly effective when taken as prescribed.
- PrEP should be integrated with HIV testing, STI screening, risk-reduction counseling, and hepatitis B assessment/vaccination when indicated.
- CDC guidance recommends informing sexually active adolescents and adults about PrEP and prescribing it to people who request it, regardless of whether they report traditional HIV risk factors.

Who Should Be Offered PrEP?

People who are HIV-negative and have potential sexual or injection-related exposure.

- Examples include sexual partners of people with HIV when viral suppression is uncertain
- MSM and transgender persons with sexual exposure;
- people with substantial heterosexual HIV exposure risk;
- people who inject drugs;
- people with recurrent STIs or recurrent PEP use; and people who request PrEP after appropriate HIV testing.
- **PrEP is prevention—not treatment—and HIV infection must be excluded before initiation.**

Current PrEP Options

- TDF/FTC — daily oral PrEP.
- TAF/FTC — daily oral PrEP.
- Long-acting cabotegravir (CAB-LA) — injection every 2 months after the initiation schedule.
- Lenacapavir (LEN) — subcutaneous injection every 6 months for PrEP.
- WHO recommended twice-yearly injectable lenacapavir as an additional HIV prevention choice in 2025.

Oral TDF/FTC

- Tenofovir disoproxil fumarate + emtricitabine.
- **Advantages**: extensive efficacy and safety data; broad clinical experience; effective for sexual and injection-related exposure; active against HBV.
- **Limitations**: daily pill burden; adherence dependence; possible renal effects; small reductions in bone mineral density.
- Clinical point: effectiveness is strongly dependent on adherence.

2+1+1 strategy

- 2+1+1 PrEP uses TDF/FTC: 2 tablets 2–24 hours before sex, then 1 tablet 24 hours later and 1 tablet 48 hours after the first dose.
- Evidence and guideline recommendations vary by population and country.
- It is primarily studied/recommended for adult MSM with anticipated intermittent sexual exposure, rather than as a universal PrEP strategy.

TAF/FTC

- Tenofovir alafenamide + emtricitabine.
- **Advantages**: lower systemic tenofovir exposure and generally less effect on renal and bone biomarkers than TDF.
- **Important limitation**: not indicated for receptive vaginal sex because efficacy data are insufficient for this population.

Long-Acting Cabotegravir

- Cabotegravir long-acting (CAB-LA) avoids daily pills.
- After the initiation injections, dosing is every 2 months.
- **Advantages**: very high efficacy and useful for people who have difficulty maintaining daily adherence.
- **Challenges**: injection-site reactions, regular clinic attendance, and a pharmacologic tail after discontinuation.
- HIV testing is particularly important; CDC recommends HIV Ag/Ab plus HIV-1 RNA testing during CAB-LA follow-up.

The Pharmacologic 'Tail' Problem

- Long-acting injectable drugs decline gradually after discontinuation.
- Drug concentrations may become insufficient to prevent HIV while remaining detectable.
- If HIV infection occurs during this period, selective drug pressure may contribute to resistance.
- Missed injections require prompt HIV testing and clinical assessment.

Why Lenacapavir?

- Lenacapavir is a first-in-class HIV capsid inhibitor.
- It has a very long half-life and can be administered subcutaneously.
- For PrEP, the regimen is twice yearly.
- The major potential advantage is reducing the adherence burden associated with daily oral PrEP.
- **WHO recommended injectable lenacapavir as an additional HIV prevention choice in 2025**

Part I — Clinical Trial Takeaways

1. Twice-Yearly Lenacapavir — A Major Shift in HIV Prevention

PURPOSE 1 & PURPOSE 2: the impressive efficacy of twice-yearly injectable lenacapavir PrEP is holding up in longer, more real-world-like follow-up.

PURPOSE 1 *cisgender women*

- 0 new HIV infections among lenacapavir recipients during the first 52 weeks of the open-label extension (OLE).
- 7,178 person-years of cumulative follow-up among lenacapavir recipients.
- 95.2% of eligible participants chose lenacapavir once given the option in the OLE.
- Injection adherence at week 52: 96%.
- No new safety signals.

PURPOSE 2 *cisgender men and gender-diverse individuals*

- 1 HIV acquisition during the open-label lenacapavir phase.
- 4 infections total over more than 5,295 person-years of lenacapavir exposure from the start of the trial.
- 92% injection adherence among participants who switched from oral F/TDF.

The key point isn't only efficacy — around 95% of participants chose long-acting lenacapavir once given the option, underlining the value of reducing pill burden, stigma and adherence demands.

Clinical implication

Long-acting PrEP should increasingly be seen as a choice-based prevention strategy, not simply a fallback for people who struggle with daily oral PrEP.

Safety of Lenacapavir

- Injection-site reactions (ISRs) are the most prominent tolerability issue.
- In PURPOSE 1, ISRs were more frequent with LEN; most were mild/moderate and only 0.2% discontinued because of ISRs.
- In PURPOSE 2, no major safety signal was identified; injection-site reactions were the most relevant adverse event.
- Long-term post-approval safety surveillance remains important as use expands.

PrEP Comparison Table

Feature	TDF/FTC	TAF/FTC	CAB-LA	LEN
Route	Oral	Oral	Injection	Injection
Frequency	Daily	Daily	Every 2 months*	Every 6 months
HBV activity	Yes	Yes	No	No
Main practical issue	Daily adherence	Daily adherence	Injection/tail	Injection/tail
Evidence base	Extensive	Extensive	Strong	Emerging/expanding

*CAB-LA requires an initiation schedule before the q2-month maintenance interval.

2025–2026 Regulatory & Guideline Update

- ***June 2025***: FDA approved injectable lenacapavir for HIV PrEP.
- ***July 2025***: WHO recommended twice-yearly injectable lenacapavir as an additional PrEP choice.
- ***September 2025***: CDC issued a clinical recommendation for injectable lenacapavir as a PrEP option.
- **CDC guidance**: LEN can be used for people weighing at least 35 kg who could benefit from PrEP, with dosing every 6 months.

Baseline Evaluation Before PrEP

- Confirm HIV-negative status with appropriate testing; use HIV-1 RNA when indicated.
- Screen for STIs according to sexual exposure and clinical context.
- Assess renal function for oral tenofovir-containing PrEP.
- Assess hepatitis B status, particularly before TDF/FTC or TAF/FTC.
- Assess pregnancy when clinically relevant.
- Discuss adherence, preferences, access, and the practical feasibility of each PrEP modality.

Follow-up During PrEP

- HIV status: regular HIV Ag/Ab testing and HIV RNA when indicated.
- STIs: periodic screening based on exposure and risk.
- Renal function: monitor for patients taking tenofovir-containing oral PrEP.
- Adherence: especially important with oral PrEP.
- Injection schedule: critical for CAB-LA and LEN.
- Review adverse effects, changes in exposure, pregnancy status when relevant, and patient preference.

Choosing a PrEP Strategy

- Consider patient preference and exposure pattern.
- Assess adherence feasibility and ability to attend injection visits.
- Consider renal and bone health.
- Consider HBV status.
- Consider pregnancy and reproductive plans when clinically relevant.
- Consider access, cost, injection acceptability, and local regulatory availability.
- PrEP should be patient-centered rather than one-size-fits-all.

Key Take-Home Messages

- PrEP is one of the most effective biomedical HIV prevention strategies.
- Choice of PrEP should be individualized.
- Adherence remains a major determinant of real-world effectiveness of oral PrEP.
- CAB-LA provides an effective long-acting alternative.
- Twice-yearly lenacapavir represents the major recent advance in HIV prevention.
- PURPOSE 1 and PURPOSE 2 demonstrated very high efficacy of twice-yearly LEN across different populations.
- HIV testing remains essential before and during PrEP.
- Long-acting PrEP introduces implementation issues, particularly injection follow-up and the pharmacologic tail.

Thank you !!!

